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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/335,461	11/07/1994	RUTH A. GIERSET		8495

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PERKINS COIE LLP
POST OFFICE BOX 1208
SEATTLE, WA 98111-1208

EXAMINER	
LOW, CHRISTOPHER S F	

ART UNIT	PAPER NUMBER
1653	38

DATE MAILED: 03/27/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

FILE COPY

Office Action Summary	Application No. 08/335,461	Applicant(s) GIERSET ET AL.	
	Examiner Christopher S. F. Low	Art Unit 1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE ____ MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 January 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4-20 and 23* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4-20 and 23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *36* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

The response filed 7 Jan 2003 has been received. In the response, an amendment to the cross reference to related applications was made and no claims were amended. Thus, claims 1, 2, 4-20 and 23 are pending. Insofar as there may have been typographical errrors on the previous PTO 326, the pending claims are indicated above and were all treated on the merits under one or both of 35 U.S.C. 102 or 35 U.S.C. 103. The following ground(s) of objection and rejection remain applicable to the pending claims.

The information disclosure statements filed 7 Jan 2003 and 18 March 2003 have been received and considered. A copy of the PTO 1449s are attached to this Office Action. Please note that one or more references have been lined through. Lined through ;references (a) have been previously cited on a PTO 1449 or PTO 892 or (b) have not been provided with the information disclosure statement or (c) are in a foreign language (e.g., French or Japanese) where there is no explanation *per se* in the information disclosure statement detailing the reasons for citation of the foreign language document(s).

Continuing Application Information

As to the amendment to the continuing data, the data is not up to date. The two applications, 08248814 and 08236221 appear to be abandoned and the current statement (response page 2, filed 7 Jan 2003) does not reflect this fact. Correction is required.

Anticipation Rejection(s)

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office Action:

> A person shall be entitled to a patent unless
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

Claims 1, 2, 4, 5, 8-15, 17-20 and 23 remain rejected under 35 U.S.C. 102(e) as being anticipated by Roth *et al.* (US 6069134 or 5747469 (equivalent to the '134 patent)). The patent disclosed and claimed claim 1 of the instant application. See for example, patented claim 3 among others. The patent teaches delivering genetic material encoding the p53 protein, expressing same (which enhances the sensitivity to the cell to the tumor therapy). Note also the teaching at column 2 regarding the issue of tumor cells with defective genetic material encoding p53. Thus, claims 1 and 2 are anticipated. As to present claim 4, the patent teaches and claims (claim 10-13) radiation as part of the therapy (note that microwave irradiation produces heat which is the same as hyperthermia - excess heat, higher temperature of present application claim 8), that chemotherapy (claims 14+) is part of the therapy. See also the paragraph bridging columns 4-5 of the patent.

Of note is that application claim 9 recites a list of cell types and tissues. The patent claim 29+ recites cell types of application claim 9 (e.g., lymphoma cells, lung carcinoma cells, sarcoma

cells). As to application claim 10, the '134 patent teaches and claims the delivery of the gene is via vector (see, e. g., claim 29+) such as an adenoviral vector, adeno-associated vector, herpes simplex based vector, retroviral based vector. The genetic material encoding p53 would have been expected to have been coupled to the virus capsid or particle in a recombinant viruses (column 3) or a liposome (patent claim 44), a polylysine glycoprotein carrier complex (patent claim 45) which also considered to be a ligand.

Claims 17-20 and 23 recite routes of administration by direct, intraarterial, intracavitary, and intravenous infusion and are anticipated by the patent teachings (see e.g., paragraph bridging columns 7 and 8, column 12, lines 52+ as to intraperitoneal (i. e., intracavitary)) and the patent claims 54+. Note that unless specifically differentiated by differences in the process results, direct, intraarterial, intracavitary, and intravenous infusion are considered as anticipated variations in intravenous administration. See also example 6 regarding intratracheal instillation wherein some degree of aerosolization is anticipated. Thus, the claims are anticipated by the reference.

Response To Amendment Argument

The response filed 7 Jan 2003 discusses the rejection for anticipation at pages 3-14. The following are noted.

- There is interfering subject matter; the art cited also claims the same subject matter; and, a table has been provided which discusses where support for the claimed invention is located in parent applications. Each is unpersuasive for the below reasons.
- The response states that neither Roth *et al.* patents US 6069134 or 5747469 (response at pages 10-11) predate the current application effective filing date. As to both of the Roth et al. and the Zhang *et al.* patents, the comments are unpersuasive regarding the combined therapy because the response points to no specific pages nor columns nor lines of any column as support for the assertion made at page 11 of the response as to no teaching regarding combined therapy. As pointed out in the stated rejection, "... the patent teaches and claims (claim 10-13) radiation as part of the therapy (note that microwave irradiation produces heat which is the same as hyperthermia - excess heat, higher temperature of present application claim 8), that chemotherapy (claims 14+) is part of the therapy ...". This is teaching of combined therapy and makes commentary in the response unpersuasive.
- There is commentary regarding 1.608(a) compliance, however, given the preceding unpersuasive commentary in the response, 37 C.F.R. 1.608(b) is applicable.
- The declaration by Gjerset under 37 C.F.R. 1.131 has been received but is inappropriate under 37 C.F.R. 1.608(b) and thus, ineffective.

The request for an interference (response at pages 12-14), identified patent(s), and proposed count(s). An interference is not applicable at this time in view of the unpersuasive commentary in the above response. The response and declaration do not antedate the references.

Rejection I under 35 U.S.C. 103

Claims 1, 2, 4-15, 17-20 and 23 remain rejected under 35 U.S.C. 103(a) as being unpatentable over by Roth *et al.* (US 6069134 or 5747469 (equivalent to the '134 patent)) taken with Moossa *et al.* (Comp. Text. Oncol., vol. 1 and 2).

Roth *et al.* is applied here as discussed above. As discussed above, the reference combines genetic therapies with conventional drug therapies described in Moossa *et al.* which would have been obvious to use because Roth *et al.* teaches use of same in connection with genetic therapy. Thus, one of ordinary skill would have known and used radiation therapy (as for example Moossa *et al.* at pages 477, 1138, 1140, and 1170), chemotherapy (as for example Moossa *et al.* at pages 527-536, 565-568, 1098, 1140, and 1572), biological therapy (as for example Moossa *et al.* at pages 607-612 using biological response modifiers), cryotherapy (as for example Moossa *et al.* at pages 1098, 1170, 1329, 1368, and 1569-1570), and hyperthermia (as for example Moossa *et al.* at page 1139-1149) are known treatment methods, have been successfully used, and are routine for one of ordinary skill in the art to have used in treating cancers either as single methods or as combined methods in various combinations as well as to have used routine methods for delivery of the therapeutic agent (as for example via an artery (page 590) or a (page 591) body cavity or by IV as for example indicated at page 592) and would have resulted in the process wherein a DNA encoding a tumor sensitizing product would have been delivered to an afflicted individual along with routine known and established appropriate therapies (radiation therapy, chemotherapy, biological therapy, cryotherapy, and hyperthermia therapy in one or more combinations) for treatment of cancers. Thus, the claimed invention was within the ordinary skill in the art to make and use at the time it was made and was as a whole, *prima facie* obvious.

Response To Amendment Argument

The response filed 7 Jan 2003 discusses the rejection for obviousness at pages 14-15 has been considered but is unpersuasive. The response in the paragraph bridging pages 14-15 presents discussion regarding the 37 C.F.R. 1.131 declaration. The declaration is unpersuasive to show a therapy on the basis of no *in vivo* results. The *in vitro* results do not appear to have been correlated to what would have been expected *in vivo*. In addition the response states that neither Roth *et al.* patents US 6069134 or 5747469 (response at pages 10-11) predate the current application effective filing date. As to both of the Roth et al. and the Zhang *et al.* patents, the comments are unpersuasive regarding the combined therapy because the response points to no specific pages nor columns nor lines of any column as support for the assertion made at page 11 of the response as to no teaching regarding combined therapy, however, "... the patent teaches and claims (claim 10-13) radiation as part of the therapy (note that microwave irradiation produces heat which is the same as hyperthermia - excess heat, higher temperature of present application claim 8), that chemotherapy (claims 14+) is part of the therapy ...". This is teaching of combined therapy and makes commentary in the response unpersuasive. The commentary regarding Moossa *et al.* and the decision on the appeal are noted but the facts are not the same. The ground of rejection and reasoning set forth differ. The patents remains as references and when combined with the Moossa *et al.* reference, makes the claimed invention obvious.

Rejection II under 35 U.S.C. 103

Claims 1, 2, 4-15, 17-20 and 23 are rejected under 35 U.S.C. 103(a) as being unpatentable over by Zhang et al. (US 6410010) taken with Moossa *et al.* (Comp. Text. Oncol., vol. 1 and 2).

Zhang *et al.* disclose administering vectors that restore wild-type p53 function (see column 3, line 25+) as a cancer therapy in cells having a mutant or aberrant p53 gene as effective methods of cancer therapy (column 5, lines 15+ as well as column 13 and 14, lines 2+ and 3+ respectively) and where palliative therapy for the patient would have been expected to have been included since (column 16, lines 29+) would indicate (line 57+) inclusion of other palliative therapies. Insofar as the patent suggests other palliative therapies, one of ordinary skill would have known and used radiation therapy (as for example Moossa *et al.* at pages 477, 1138, 1140, and 1170), chemotherapy (as for example Moossa *et al.* at pages 527-536, 565-568, 1098, 1140, and 1572), biological therapy (as for example Moossa *et al.* at pages 607-612 using biological response modifiers), cryotherapy (as for example Moossa *et al.* at pages 1098, 1170, 1329, 1368, and 1569-1570), and hyperthermia (as for example Moossa *et al.* at page 1139-1149) are known treatment methods, have been successfully used, and are routine for one of ordinary skill in the art to have used in treating cancers either as single methods or as combined methods in various combinations as well as to have used routine methods for delivery of the therapeutic agent (as for example via an artery (page 590) or a (page 591) body cavity or by IV as for example indicated at page 592) and would have resulted in the process wherein a DNA encoding a tumor sensitizing product would have been delivered to an afflicted individual along with routine known and established appropriate therapies (radiation therapy, chemotherapy, biological therapy, cryotherapy, and hyperthermia therapy in one or more combinations) for treatment of cancers and would (Zhang *et al.*, column 16) have been expected to have increased the therapeutic effect of the treatment based on at least the longer period of time the patient would have been expected to have remained alive. Thus, the claimed invention was within the ordinary skill in the art to make and use at the time it was made and was as a whole, *prima facie* obvious

Response To Amendment Argument

The response filed 7 Jan 2003 discusses the rejection for anticipation at pages 16-18. The following are noted. The response at pages 16-17 presents discussion regarding the inappropriate nature of the 37 C.F.R. 1.131 declaration. The response comments regarding the Zhang *et al.* patent are unpersuasive because (column 2, line 60+) indicates providing efficient means to restore p53 functions by (column 3, line 25+) introducing wild type p53 genes into target cells (obviously the wild type gene encodes the wild type p53) and is unexpectedly effective in inhibiting the growth of lung cancer cells (column 3, line 38+) with astonishing efficacy (column 3, line 40-45). See also column 5, line 15+) and would not preclude the patient from receiving other palliative therapy (column 16, line 57+). For at least these reasons, the comments in the response at pages 16-18 are unpersuasive. Given the combined teachings of Zhang *et al.* and Moossa *et al.*, the claimed invention stands rejected as obvious.

Rejection III under 35 U.S.C. 103

Claim 16 is rejected under 35 U.S.C. 103 as being unpatentable over Roth *et al.* (US 6069134 or 5747469 (equivalent to the '134 patent)) taken with Moossa *et al.* (Comp. Text. Oncol., vol. 1 and 2) as applied to claims 1, 2, 4-15, 17-20 and 23 above and further in view of Wu *et al.* (US '320); or, Zhang et al. (US 6410010) taken with Moossa *et al.* (Comp. Text. Oncol., vol. 1 and 2) as applied to claims 1, 2, 4-15, 17-20 and 23 above and further in view of Wu *et al.* Roth *et al.* and Zhang *et al.* are newly cited and the latter two references are of record.

Roth *et al.* (US 6069134) taken with Moossa *et al.* (Comp. Text. Oncol., vol. 1 and 2); and, Zhang et al. (US 6410010) taken with Moossa *et al.* are applied as indicated above and where Roth et al. on the one hand and Zhang et al. on the other hand both teach various vectors and conjugation and/or encapsulation of the vectors, Wu *et al.* disclose a process for *in vivo* delivery (as for example intravenous injection, i.e., a direct injection wherein injection into an artery is an obvious variation of injection into a vein) of DNA to a target cell (see for example column 11, and the abstract as to polylysine) using a complex of asialoglycoprotein to hepatoma cells and for replacement of "defective genes" such as the DNA encoding p53. Thus, the claimed invention was within the ordinary skill in the art to make and use at the time it was made and was as a whole, *prima facie* obvious.

Response To Amendment Argument

The response filed 7 Jan 2003 discusses the rejection for anticipation at pages 18. The following are noted. The comments regarding the Roth *et al.* and the Zhang *et al.* patents have been considered above and were unpersuasive. The comments remain unpersuasive here even where at page 19 the response asserts that the Wu *et al.* reference adds nothing. Wu *et al.* was cited for disclosure of a process for *in vivo* delivery (as for example intravenous injection, i.e., a direct injection wherein injection into an artery is an obvious variation of injection into a vein) of DNA to a target cell (see for example column 11, and the abstract as to polylysine) using a complex of asialoglycoprotein to hepatoma cells and for replacement of "defective genes" such as the DNA encoding p53. Thus, the comments at page 18 ;are unpersuasive.

Gjerset Declaration Filed Under 37 C.F.R. 1.131

The response page 19 commentary about the Gjerset declaration filed under 37 C.F.R. 1.131 has been considered. The declaration as pointed out earlier is ineffective as filed. The statement needs to be made under 37 C.F.R. 11.608(b). See also M.P.E.P. 715. From the present response it would appear that applicant recognizes this issue but has filed the declaration using the incorrect section of the Code of Federal Regulations.

In addition, the current claims are or appear to be directed to an *in vivo* process of treating cancer. The declaration *per se* provides no apparent discussion of the *in vitro* results and nexus to *in vivo* results. For the above reasons the comments at page 19 are unpersuasive.

No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. 1.136(a).

A shortened statutory period for response to this final action is set to expire THREE MONTHS from the date of this action. In the event a first response is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 C.F.R. 1.136(a) will be calculated from the mailing date of the advisory action. In no event will the statutory period for response expire later than SIX MONTHS from the date of this final action.

CSFL
25 Mar 2003

CHRISTOPHER S. F. LOW
SUPERVISORY PATENT EXAMINER
GROUP 1600